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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,185	10/21/2005	Mark T Bilodeau	21377YP	1883
210 7590 05/11/2009 MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907				
EXAMINER				
CHANG, CELIA C				
ART UNIT		PAPER NUMBER		
1625				
MAIL DATE		DELIVERY MODE		
05/11/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/554,185

Applicant(s)

BILODEAU ET AL.

Examiner

Celia Chang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 January 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Amendment and response filed by applicants dated Jan. 21, 2009 have been entered and considered carefully.

Claims 9-18 have been canceled. Claims 1-8 are pending.

Applicants argued that the Patani reference was not made available to applicants. A copy of the reference is hereby attached.

2. The rejection of claims 1-8 under 35 USC 103(a) over Bilodeau et al. '738 in view of King, Webber and Patani is maintained for reason of record.

A clear delineation of that replacement of a phenyl ring structure with its *bioisosteric* thiophenyl ring structure is considered structural *prima facie* obvious.

Applicants argued that there seemed to be some unpredictability in isosteric replacement and thiophene/benzene isostere may not elicit the same biological activity. Although King et al. on p.209 disclosed possible variation when isostere was replaced, it also taught that even with possible variation success is well known i.e. see same page 209, last 4 lines of the first paragraph: *A more detailed discussion of this topic is beyond the scope of this chapter, but the reader is directed to the excellent reviews by Thornber¹ and Lipinski² where numerous examples of successful isosteric and bioisosteric replacements are listed.*

The success therefore is well known especially with the thiophene and benzene pair, See Patani et al. p. 3158, section on ring equivalents; Webber et al. whole article and structural analysis on the thiophene and benzene ring, especially in a fused ring system as the claims. The motivation for one skilled in the art is the modification is an "rational" approach in medicinal chemistry (see Patani p.3147 right column). Prior art has evidenced that such a rational approach has been repeated taught in medicinal chemistry wherein King is dated 1994, Webber is dated 1995, Patani is dated 1996 and in more recent publication Siebert in 2004 wherein successful bioisosteric replacement on variations of compounds have been documented (see p.321 and English summary p.324). In the decision of *Mead Johnson v. Premo Pharm.* 207 USPQ 820, the court has set forth that "Drug design is the attempt by medicinal chemists... One of the methods of drug design is the molecular modification of an existing biologically active

compound by changing certain portions of the molecular structure of the original or "lead" compound....The medicinal chemists in 1955 would utilize a rational approach to drug design...." (see p.830). Therefore, such rational, choice and motivation finding iboisosteric replacement being prima facie obvious of a lead compound is very clearly delineated.

In the Bilodeau '738 reference, it was clearly disclosed that at col. 68-69, scheme 5, the detailed process of how to make the lead compound, at col. 111-112, 2nd compound, explicit delineation of the structure of the lead compound, and at col. 131 lines 39-42, clear description that the compound made in scheme 5, table 6 have been tested with biological activity. Therefore, the prior art clearly disclosed a lead compound. The state of the art after 1955 have been continuously supported the success and rational design choice in modifying lead compound with its bioisostere. Absent of unexpected result, the teaching, suggestion and motivation have well been provided in the prior art to establish a prima facie case of obviousness.

3. The same argument was presented by applicants with respect to the obviousness type double patenting rejection. Based on the same evidence as found in section 2, the rejection of claims 1-8 under the judicially created doctrine of obviousness type double patenting is also maintained for reason of record.
4. The rejections could have been made final since the same identical issues were clearly delineated in the previous office action. Applicants are urged to call the examiner were any of the references missing and a copy would be provided, so that applicants can respond completely with all evidence discussed.
5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

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may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
May 7, 2009

/Celia Chang/
Primary Examiner
Art Unit 1625